II. Requirement for Abstract

The Examiner has remarked that "[a]n abstract is required, and does not appear to have been submitted." (Office Action dated June 26, 2001, page 2, line 12.) Although an abstract was included in Applicants' original filing, as is evidenced by the first page of the International publication of the application, Applicants now provide an abstract on a separate page. Applicants thank the Examiner for bringing this to Applicants' attention and provide the abstract as an attachment to this response.

III. Rejection Under 35 U.S.C. § 112, First Paragraph

In the Office Action, claims 17-24 and 32 have been rejected under 35 U.S.C. § 112, first paragraph, as indefinite for failing to point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants respectfully traverse these rejections for the reasons detailed below.

The Office Action alleges that the rejected claims 17-24 and 32 "contain[ ] subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." (Office Action dated June 26, 2001, page 2, line 19—page 3, line 2). Applicants respectfully disagree.

For an enablement rejection to be proper, "it is incumbent upon the Patent Office ... to explain *why* it doubts the truth or accuracy of any statement in a supporting

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disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." M.P.E.P. § 2164.04 (emphasis in original). Because all patent applications are presumptively valid, *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971), the Examiner must accept as true Applicants' statements concerning utility, "unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P § 2164.04 In the present case, Applicants respectfully submit that the evidence enabling one of ordinary skill in the art to make and use the present invention that is provided in the specification should be accepted as true in favor of the allegation made in the Office Action.

With respect to the disclosure in the specification concerning how to make the claimed compounds, no reasoning or support is provided in the Office Action as to *why* Applicants' disclosure is insufficient. To the contrary, the specification discloses twenty-three examples of how to prepare the claimed compounds and a twenty-fourth example listing thirteen additional compounds that can be prepared by analogous methods. (Specification, pages 13-65.) Applicants submit that these examples are sufficient to enable the entire scope of the claims. Accordingly, Applicants respectfully request withdrawal of the § 112, first paragraph, rejection at least wherein the rejection is based on the proposition that the specification does not enable one of ordinary skill in the art to make the claimed compounds.

With respect to the disclosure in the specification concerning how to use the claimed compounds, the Office Action provides reasons, albeit insufficient, asserting

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why the statements in the specification are doubted, however, no support is given to *back up* these bald assertions. Specifically, the Office Action alleges that "[i]t may be the case that the claimed compounds are analogous to other compounds which have been shown to inhibit bacterial growth. However, even small changes in structure can lead to dramatic changes in activity, or obliteration of activity" because "[t]he reality in pharmacology is that one cannot predict activity merely by viewing a structure." (Office Action dated June 26, 2001, page 3, lines 4-8.) Applicants respectfully submit that this reasoning is insufficient to rebut the presumption of utility provided by Applicants' disclosure.

The *Manual of Patent Examining Procedure* ("*MPEP*") provides that at least eight independent factors can be considered by the Examiner in his determination of non-enablement. M.P.E.P § 2164.01(a) (citing *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Although the Examiner is not required to discuss each and every one of the *Wands* factors, he must "focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation." M.P.E.P. § 2164.04 (emphasis in original). The reasoning provided in the Office Action does not comply with the standard set forth in *Wands*.

Additionally, in comparison with the several *prima facie* cases of non-enablement found in the *Training Materials for Examining Patent Applications with Respect to 35 U.S.C. Section 112, First Paragraph-Enablement Chemical/Biotechnical Applications* ("*PTO Enablement Training Manual*"), released by the PTO as guidance in August,

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1996, excerpt enclosed herewith, Applicants submit that the present application and the surrounding circumstances provide much more basis for finding a sufficient demonstration of utility.

Specifically relevant to the present case, Applicants refer the Examiner to "*Example 5E: Peptides for Treating Obesity.*" As does Applicants' specification, the specification in this example disclosed compositions and, for treating obesity, a "pharmaceutical formulation" comprising such compositions and a "pharmaceutically acceptable carrier" for such compositions. Additionally, the specification of the Example disclosed "several routes of administration but no dosages, not even general ranges." It also disclosed suitable test animals and how to carry out the animal model tests, but did not disclose whether such tests were done using the peptide of the invention. There were no structurally similar peptides known in the prior art for treating obesity. The specification provided further that the peptides could be used as an additive in animal feed and that it was well established in the art how this could be done.

In the example, the PTO determined that claims directed to the compounds themselves were enabled because the disclosure of one enabled use in the specification (additive in animal feed) was sufficient to support a claim that was not directed to a specific use. The "pharmaceutical" and "pharmaceutically acceptable" language, however, required more. The PTO determined that the state of the prior art (lack of a teaching that the proteins of the prior art could be used to treat obesity) coupled with the applicant's failure to disclose dosages or working examples would

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result in undue experimentation. To cure the defect, the PTO suggested that the terms "pharmaceutical" and "pharmaceutically acceptable" be deleted from the claims.

In contrast with the referenced example, Applicants' specification discloses several routes of administration (for example, see page 65, lines 21-23) and dosages (for example, see page 67, lines 18-28). Applicants also disclose a working example of tablets comprising such dosage that could, for example, be made. (Specification, page 68, lines 3-12.) Further, Applicants disclose several references that establish that streptogramins are a recognized class of antibacterials. (Specification, page 2, line 7—page 3, line 5.) Even further, Applicants provide a disclosure of *in vivo* dosing and results (for example, see page 11, lines 20-25), low toxicity results (for example, see page 11, lines 26—page 12, line 2), and metabolic stability results (for example, see page 8, lines 12-19). In the present Office Action, neither reasoning nor support for such reasoning is provided for doubting these disclosures by Applicants.

Applicants submit that whereas the state of the prior art in the PTO example suggested a lack of predictability and the applicant's specification there lacked guidance, neither circumstance is present in this case. Applicants submit that, if the Examiner were to analyze the present case using the *Wands* factors, he would find that Applicants provide "considerable direction and guidance in the specification," that there "was a high level of skill in the art at the time the application was filed," and that "all of the methods needed to practice the invention were well known," just as in *Wands*. M.P.E.P. § 2164.01(a) (citation omitted).

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Further, Applicants note that the Examiner's suggestion that Applicants submit "*in vitro* data that establishes the [bacterial] growth inhibitory efficacy that has been asserted" (Office Action dated June 26, 2001, page 3, lines 9-10) is misplaced, as Applicants are not required to provide such data unless and until the Examiner has established a *prima facie* case of non-enablement. M.P.E.P. § 2164.05.

As the Examiner has failed to establish a *prima facie* case of non-enablement, Applicants respectfully request withdrawal of the rejection under § 112, first paragraph.

IV. Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 17-24 and 32 under 35 U.S.C. § 112, second paragraph, as indefinite for failing to point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants respectfully traverse these reasons for rejection for the reasons detailed below.

In any § 112, second paragraph, rejection, the Manual of Patent Examining Procedure ("*MPEP*") provides that, if the scope of the invention can be determined from the language of the claims with a reasonable degree of certainty, then any rejection under 35 U.S.C. § 112, second paragraph, is improper. M.P.E.P. § 2173.02 (emphasis in original). Applicants respectfully submit that the present claims meet this statutory standard for the reasons set forth below. Accordingly, Applicants request withdrawal of all rejections under § 112, second paragraph.

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The Examiner has rejected claim 17 for "mak[ing] reference to 'R' and 'S' epimers, without identifying which carbon is at issue." (Office Action dated June 26, 2001, page 3, lines 16-17.) Applicants respectfully disagree that their original claim language is unclear or indefinite and accordingly traverse this rejection.

The Examiner notes that "[p]resumably it is the carbon bearing R_1." (Office Action dated June 26, 2001, page 3, line 17.) Applicants submit that it is blatantly clear that the carbon at issue is the carbon bearing R_1 and that one of ordinary skill in the art would know this because the claims as originally filed are clear. For example, Applicants' specification shows where the group $\sim\!\!\sim R_1$ is positioned. (Specification, page 1, formula (I).) As a further example, the specification provides that this group is bonded to the carbon at the 16 position. (Specification, page 3, lines 6-14.) Even further, for example, the specification provides that epimers can be formed on the 16 position. (Specification, page 7, lines 18-24.) Accordingly, Applicants submit that it would be clear to one of ordinary skill in the art that a chiral carbon atom can be the carbon at the 16 position, which bears the group $\sim\!\!\sim R_1$. To advance prosecution, however, Applicants have amended claim 17 in accordance with the Examiner's suggestion for further clarification. Applicants thank the Examiner for this suggestion and respectfully request that this ground for rejection be withdrawn.

The Examiner has also rejected claim 17 as indefinite for being drawn to one compound, while simultaneously referring to mixtures of compounds. (Office Action dated June 26, 2001, page 3, lines 18-19.) Applicants respectfully traverse this

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rejection as their original claim language is clear, however, to advance prosecution, Applicants have amended claim 17 further in accordance with the Examiner's suggestion. Specifically, Applicants have "amend[ed] claim 17 to make it clear that compounds, salts and mixtures of stereoisomers of the compounds are being claimed." (Office Action dated June 26, 2001, page 4, lines 14-15.) Applicants thank the Examiner for this suggestion and respectfully request that this ground for rejection be withdrawn.

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V. Conclusi n

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: September 28, 2001

By _____
Michele L. Mayberry
Reg. No. 45,644

Attachments: Excerpt (Example 5E) from *PTO Enablement Training Manual*
Appendix to Amendment
Abstract

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Application Number: 09/492,392
Filing Date: January 27, 2000
Attorney Docket Number: 3806.0464.00

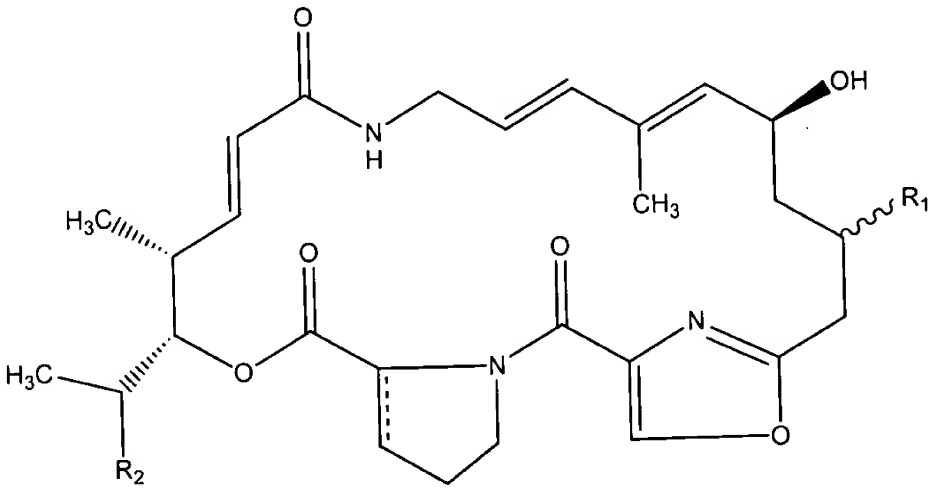
APPENDIX TO AMENDMENT OF SEPTEMBER 28, 2001

Version with Markings to Show Changes Made

IN THE CLAIMS:

Please replace claims 17-19 with amended claims 17-19, as follows:

17. (Once Amended) A group A streptogramin derivative ~~of formula (I) or a salt thereof~~ **chosen from group A streptogramin derivatives of formula (I), salts thereof, and mixtures of stereoisomers of any of the foregoing**:



(I)

wherein:

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- R_1 is chosen from -NR'R" groups, wherein
  - R' is chosen from a hydrogen atom and a methyl group, and
  - R" is chosen from
    - (i) a hydrogen atom,
    - (ii) alkyl groups,
    - (iii) cycloalkyl groups,
    - (iv) an allyl group,
    - (v) a propynyl group,
    - (vi) a benzyl group,
    - (vii) -OR"' groups, wherein R"' is chosen from a hydrogen atom, alkyl groups, cycloalkyl groups, an allyl group, a propynyl group, and a benzyl group, and
    - (viii) $-NR_3R_4$ groups, wherein
      - R_3 and R_4 are each a methyl group, or
      - R_3 and R_4, which are identical or different, form, together with the nitrogen atom to which they are attached, a saturated or unsaturated 4- to 5-membered heterocyclyl group, wherein one of said members, in addition to said nitrogen atom, may be an atom chosen from an oxygen atom, a sulphur atom, and a nitrogen atom,

- R_2 is chosen from a hydrogen atom, a methyl group, and an ethyl group,

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- the bond ---- is a single bond or a double bond,

- unless otherwise stated, said alkyl groups are chosen from straight and branched C_1-C_6 alkyl groups,

- unless otherwise stated, said cycloalkyl groups are chosen from C_3-C_4 cycloalkyl groups,

~~- when R" is chosen from a group other than said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivative is chosen from R-epimers and R- and S- epimers, wherein said R-epimer is predominant, and~~

~~- when R" is chosen from said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivative is chosen from R-epimers, S-epimers, and mixtures of R- and S-epimers.~~

- when said R" is chosen from a hydrogen atom, alkyl groups, cycloalkyl groups, an allyl group, a propynyl group, and a benzyl group, said group A streptogramin derivatives and said salts thereof are chosen such that th carbon bearing said R_1 is of the R configuration and said mixtures comprise stereoisomers, wherein the carbon bearing R_1 is of th R

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configuration or the S configuration and wher in said R configuration is predominant, and

- when R" is chosen from said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivatives and said salts thereof are chosen such that the carbon bearing said R_1 is of the R configuration or the S configuration and said mixtures comprise stereoisomers, wherein the carbon bearing R_1 is of the R configuration or the S configuration.

18. (Once Amended) A group A streptogramin derivative according to claim 17, wherein:

- R_1 is chosen from -NR'R" groups, wherein
  - R' is chosen from a hydrogen atom and a methyl group, and
  - R" is chosen from
    - (i) a hydrogen atom,
    - (ii) alkyl groups,
    - (iii) cycloalkyl groups,
    - (iv) an allyl group,
    - (v) a propynyl group,
    - (vi) a benzyl group,
    - (vii) -OR"' groups, wherein R"' is chosen from C_1-C_6 alkyl groups, an allyl group, and a propynyl group,
    - (viii) -NR_3R_4 groups, wherein

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- R_3 and R_4 are each a methyl group, or
- R_3 and R_4, which are identical or different, form, together with the nitrogen atom to which they are attached, a saturated or unsaturated 4- to 5-membered heterocyclyl group, wherein one of said members, in addition to said nitrogen atom, may be an atom chosen from an oxygen atom, a sulphur atom, and a nitrogen atom,

- R_2 is chosen from a hydrogen atom, a methyl group, and an ethyl group,

- the bond ---- is a single bond or a double bond,

~~- when R" is chosen from a group other than said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivative is chosen from R-epimers and R- and S- epimers, wherein said R-epimer is predominant, and~~

~~- when R" is chosen from said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivative is chosen from R-epimers, S-epimers, and mixtures of R- and S-epimers.~~

- when said R" is chosen from a hydrogen atom, alkyl groups, cycloalkyl gr ups, an allyl group, a propynyl group, and a benzyl group, said gr up A streptogramin d rivatives and said salts th r of ar chosen such that the

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carb n bearing said R_1 is of the R configuration and said mixtures comprise stereoisomers, wherein the carbon bearing R_1 is of th R configuration or the S configuration and wherein said R configuration is predominant, and

- when R" is chosen from said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivatives and said salts thereof are chosen such that the carbon bearing said R_1 is of the R configuration or the S configuration and said mixtures comprise stereoisomers, wherein the carbon bearing R_1 is of the R configuration or the S configuration.

19. (Once Amended) A group A streptogramin derivative according to claim 17, wherein:

- R_1 is chosen from -NR'R" groups, wherein
  - R' is chosen from a hydrogen atom and a methyl group, and
  - R" is chosen from
    - (i) a hydrogen atom,
    - (ii) C_1-C_4 alkyl groups,
    - (iii) cycloalkyl groups,
    - (iv) an allyl group,
    - (v) a propynyl group,
    - (vi) a benzyl group,

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(vii) -OR"' groups, w herein R"' is chosen from C_1-C_3 alkyl groups, an allyl group, and a propynyl group,

(viii) -NR_3R_4 groups, wherein

- R_3 and R_4, which are identical or different, form, together with the nitrogen atom to which they are attached, a 5-membered saturated heterocyclyl group,

- R_2 is chosen from a methyl group and an ethyl group,

- the bond ---- is a single bond or a double bond,

~~- when R" is chosen from a group other than said -OR"' groups and said -NR_3R_4- groups, said group A streptogramin derivative is chosen from R-epimers and R- and S - epimers, wherein said R-epimer is predominant, and~~

~~- when R" is chosen from said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivative is chosen from R-epimers, S-epimers, and mixtures of R- and S-epimers.~~

- when said R" is chosen from a hydrogen atom, alkyl groups, cycloalkyl groups, an allyl group, a propynyl group, and a benzyl group, said group A strept gramin derivatives and said salts thereof are chosen such that the carb n b aring said R_1 is f the R configuration and said mixtures

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comprise st r oisomers, wherein th carbon b aring R_1 is of the R configuration or the S configuration and wherein said R configurati n is predominant, and

- when R" is chosen from said -OR"' groups and said -NR_3R_4 groups, said group A streptogramin derivatives and said salts thereof are chosen such that the carbon bearing said R_1 is of the R configuration or the S configuration and said mixtures comprise stereoisomers, wherein the carbon bearing R_1 is of the R configuration or the S configuration.

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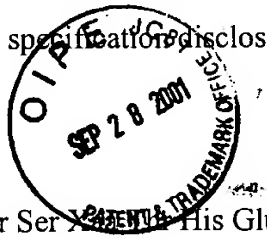
3. Example 5E: Peptides for Treating Obesity



Specification: The specification discloses an anti-obesity peptide having the following amino acid sequence:

1 5 10 15

Phe Ile Gly His Thr Ser Xaa His Glu Xaa Phe Ala Thr Xaa Trp Glu Leu Leu (SEQ ID NO 1).

Where:

Xaa at position 7 is Gln, Ile, or Met;
Xaa at position 11 is Asp, Gln, or Glu; and
Xaa at position 15 is Ser or Pro.

Preferably,

Xaa at position 7 is Ile;
Xaa at position 11 is Glu; and
Xaa at position 15 is Ser.

The specification also discloses a pharmaceutical formulation comprising the peptide of SEQ ID NO 1 and a pharmaceutically acceptable carrier, diluent, and/or excipient, as well as a method of treating obesity by administering the peptide of SEQ ID NO 1 to an obese mammal, such as mice or humans. Several routes of administration are disclosed but no dosages, not even general ranges, are disclosed.

The specification states that the peptide can be made by recombinant DNA technology or well known peptide synthesis procedures. Furthermore, the specification lists DNA sequences, vectors, host cells, and isolation techniques suitable for producing the peptide by recombinant DNA technology as well as specific peptide synthesis techniques suitable for producing the peptide.

The application discloses but does not exemplify that the peptide is a fragment of a larger protein produced in adipose tissue. The application also discloses but does not exemplify that the peptide is able to control body weight gain in normal and obese subjects. The specification discloses that suitable test animals include normal mice and obese mice, especially the ob/ob mouse model of obesity and diabetes, which is disclosed as being generally accepted in the art as being indicative of the obesity condition. The specification discloses how to carry out the animal model tests but fails to disclose whether such tests were done using the peptide of the invention. The specification also goes on to state that the peptide is also useful in the production of antibodies for diagnostic use and, as a peptide, is useful as feed additives for animals.

Claims:

1. 1. A peptide consisting of the sequence

   1 5 10 15

Phe Ile Gly His Thr Ser Xaa Thr His Glu Xaa Phe Ala Thr Xaa Trp Glu Leu Leu (SEQ ID No. 1), wherein

Xaa at position 7 is Gln, Ile, or Met;
Xaa at position 11 is Asp, Gln, or Glu; and
Xaa at position 15 is Ser or Pro.

2. The peptide of claim 1 wherein Xaa at position 7 is Ile; Xaa at position 11 is Glu; and Xaa at position 15 is Ser.
3. A pharmaceutical composition comprising the peptide of claim 1 and a pharmaceutically acceptable carrier.
4. A pharmaceutical composition comprising the peptide of claim 2 and a pharmaceutically acceptable carrier.
5. A method of treating obesity, which comprises administering to a mammal in need thereof the peptide of claim 1.
6. A method of treating obesity, which comprises administering to a mammal in need thereof the peptide of claim 2.

State of the Prior Art: There are no structurally similar peptides known in the art for treating obesity. There are other proteins that the art suggests play a role in obesity. The following references establish the state of the art with respect to such proteins.

Zhang et al, Nature, Vol. 372, pp. 425-432, December 1994.

Rink, Nature, Vol. 372, pp. 406-407, December 1994.

Marx, Science, Vol. 266, pp. 1477-1478, December 1994.

It is well established in the art how to use proteins and peptides as additives in animal feed.

Analysis:

The specification clearly teaches how to make all the peptides and compositions encompassed by the claims. Therefore, "how to make" is not an issue with any of the claims.

With respect to claims 1-2, the fact that the specification discloses that the peptides can be used as an additive to animal feed in combination with the fact that it is well established in the art how to use proteins and peptides as additives in animal feed leads to a conclusion that the specification also teaches how to use the entire scope of peptides recited in claims 1-2. Since no specific use is recited in these claims, one enabled use that covers the full scope of the claims is sufficient to preclude an enablement rejection of a compound claim based on the failure to teach "how to use".

With respect to claims 3-4, the "pharmaceutical" and "pharmaceutically acceptable carrier" language in combination with the fact that the only disclosed pharmaceutical use of the compositions is for treating obesity leads to the conclusion that these claims should be evaluated in terms of whether the specification teaches how to use the compositions for treating obesity. Since method claims 5-6 must be evaluated in terms of the recited use,

treating obesity, claims 3-6 should be evaluated together. In this case, the art noted above teaches that few medical problems have proved to be more intractable than obesity (Marx). Furthermore, even though other proteins are suggested as playing a role in obesity (Zhang), the art, such as Rink and Marx, suggest that it is not even known how to use these proteins for treating obesity. This state of the prior art suggests a lack of predictability in this art which, taken with the fact that there is a lack of guidance with respect to dosages and a lack of working examples, leads to the conclusion that it would require undue experimentation to use the invention of claims 3-6. With respect to claims 3-4, it is also noted that if the "pharmaceutical" and "pharmaceutically acceptable" language was deleted from the claims, the analysis would be the same as that set forth above with respect to claims 1-2. Therefore, an enablement rejection using form paragraph 7.31.02 of claims 3-6 would be appropriate along with a suggestion to remove the "pharmaceutical" and "pharmaceutically acceptable" language from claims 3-4 to overcome the rejection with respect to these claims.

Rejection:

Claims 3-6 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertain, or with which it is most nearly connected, to use the invention.

Claims 3-6 recite pharmaceutical compositions and methods of treating obesity using certain specific peptides. However, the specification fails to disclose any dosages for use in treating obesity. Furthermore, while the specification sets forth tests for assay anti-obesity activity of the peptides, the specification fails to provide any indication that such tests were done. Therefore, the specification also fails to provide any working examples. Marx states that few "medical problems have proved to be more intractable than obesity" and even though other proteins are suggested as playing a role in obesity (Zhang), the art, such as Rink and Marx, suggest that it is not even known how to use these proteins for treating obesity and that there is much more to be done before obesity can be treated using such proteins. In view of the intractable nature and unpredictability of treating obesity and the lack of guidance with respect to dosages and the lack of working examples, one skilled in the art could not use the inventions of claims 3-6 without undue experimentation. Note, removing "pharmaceutical" and "pharmaceutically acceptable" from claims 3-4 would overcome the rejection of these claims since one would know how to use such compositions as additives in animal feed as disclosed in the specification.

Modifications to the Above Facts: Let us assume that in addition to the above facts, the specification actually stated "The disclosed animal model assays were carried out using the peptides of the invention and the peptides were active in at least one of the assays. Therefore, the peptides are useful in treating obesity and those disorders implicated by obesity." Does this change the analysis set forth above? For claims 1-2, the answer is no. For claims 3-6, the answer is yes. Specifically, if the assays are reasonably correlative to treatment in other mammals such a statement would constitute the presence of working examples, even without the specific data. In this case, since specific dosages are not disclosed generally or in the examples, the only issue remaining is whether it would require an undue amount of experimentation to determine the proper dosages based on the examples and the state of the prior art and any enablement rejection must address this issue. If the assays do not reasonably correlate to treatment in other mammals based on the state of the art, this issue would have to be raised along with the other issues noted in the analysis and rejection above.

Note, taking the position that the assays are reasonably correlative to treatment in other mammals, it is proper to accept as being true the statement that the peptides were active in the assays, even in the absence of specific data. The Office must accept as being true the statements supporting enablement unless there is an objective reason, usually supported with documentary evidence, to question them, i.e., the burden is on the Office to demonstrate that there is an objective reason, usually supported by documentary evidence, to question the statement. Here, there is no evidence indicating that the peptides were not active in the assays. However, this analysis does not necessarily apply to other issues, such as a showing of unexpected results so as to overcome a rejection under 35 U.S.C. 103. In that case, a statement that the assays demonstrated unexpected results for the inventive peptides, in the absence of the specific results, would not be persuasive since it is applicant's burden to rebut the prima facie case of obviousness and the Office cannot determine whether applicant has met that burden without the results being present.